

The presence in foodstuffs of substances having specific harmful effects under certain conditions. By EDWARD MELLANBY.

(1) *A substance interfering with calcification.*

Interference with calcification of bones has been demonstrated to be a special property of cereals(1). When puppies eat diets deficient in the calcifying vitamin, the calcification of the bones becomes worse, the greater the amount of cereal eaten. There are also great differences among cereals themselves in their power to inhibit calcification(2). Oatmeal, although containing more calcium and phosphorus than other cereals tested, is the most potent, and white flour the least potent, in this respect. Up to the present it has not been possible either to isolate or to gain any insight into the nature of the substance responsible for this effect. Some of its properties have been dealt with elsewhere. New properties which seem to establish it as a definite entity are, (1) if oatmeal is boiled with 1 p.c. hydrochloric acid until the starch is hydrolysed and the mixture is then neutralised with soda, the substance interfering with calcification is apparently destroyed, (2) if oats are allowed to germinate for 1, 3 or 6 days (in each case after 2 days' steeping) and then heated at 100° C. for 18 hours, the power of the cereal to prevent bone calcification is reduced. Both germination and heat are necessary to get the best result, and the longer the time of germination the less does the product interfere with calcium deposition. For instance, 6 days' germination and drying by heat results in a cereal product which is at least as good as and probably better than white flour as regards bone formation. Heat alone at 100° C. has practically no destructive effect and germination alone has but slight influence. The same facts apply to barley and probably other cereals. Germinated and kilned barley is comparatively good as a cereal product from the point of view of bone formation and much better than the original barley. These results suggest most strongly that a substance in cereals having a positive interfering effect on calcification of bone has been destroyed. Oats heated with 1 p.c. sodium hydroxide for one hour still contain the substance.

(2) *A substance interfering with the nervous system.*

A second type of specific harmful effect produced by diet is that in which severe nervous symptoms are produced. In 1916 Hart, Miller and MacCollum(3) described symptoms, not unlike those recorded for beri-beri, produced in pigs by diets containing wheat and wheat embryo. They said these were due to a toxic substance in the fat of wheat embryo.

If wheat germ is added to a diet deficient in fat-soluble vitamins to the extent of 10 p.c. of the cereal, puppies often develop severe nervous symptoms after two or three months of the diet. The symptoms may be so widespread that it is difficult to describe them. The most obvious is incoordination.

The action is prevented by butter and cod liver oil and probably other sources of fat-soluble vitamin. It is also reduced in intensity by the addition of calcium carbonate to the diet. Boiling wheat germ for 1 hour in 1 p.c. hydrochloric acid also reduces the symptoms.

In my experience the major nervous lesions are more central than those indicated by Hart, Miller and MacCollum, who described changes only in the anterior lower cells and seemed to think that they were dealing with a type of beri-beri.

A condition of sub-acute combined degeneration of the spinal cord may be produced in these animals and can be seen by Marchis' stain. The brains have not been examined yet for degenerative changes but the intensity of the nervous symptoms suggests that these will be large. The changes in the cord and the nervous symptoms are similar in many respects to those that develop in pellagra and ergotism and the experimental results suggest that these pathological conditions are due in part to a similar toxic factor eaten under conditions which allow the specific nervous effect to be produced.

The above are two instances in which harmful effects are apparently produced by dietetic ingredients under certain conditions. The effects of these substances are counteracted by fat-soluble vitamins and until their chemical composition is known might therefore be described as "Toxamins."

- (1) E. Mellanby. Special Report Series, Medical Research Council. Nos. 61 and 93.
- (2) E. Mellanby. Brit. Med. Journ. 1922, Nov. 4.
- (3) Hart, Miller and MacCollum. Journ. Biol. Chem. 25. 239. 1916.

